In the Official Action, the Examiner suggested guidelines for the preferred layout for the present patent application, and Applicants have amended the specification in accordance therewith.

In addition, the Examiner indicated that the application did not comply with the sequence rules, and Applicants have amended the specification by making reference to sequence ID numbers where necessary and by providing an amended Sequence Listing in accordance with the Notice to Comply with the sequence rules. With regard to the drawing figures, Applicants will review these figures and will make appropriate reference to the correct Sequence ID numbers in the legend before formal drawings become due.

In the Official Action, the Examiner rejected Claims 54-78 under 35 U.S.C. § 112, first paragraph, on the grounds that the specification, while being enabling for a Tbp2 receptor of SEQ ID NO:2 and 4 did not "reasonably provide the full scope of enablement for derivatives of Tbp2 receptor" because of the recitation of "derived." This rejection is respectfully traversed in that it appears to be based upon the Examiner's misinterpretation of the claim language. In the first place, Claim 54 and its dependent claims do not encompass any Tbp2 derivatives or variants as asserted by the Examiner. Instead, these claims are only directed to fragments of the Tbp2 subunit of the transferrin receptor of N. meningitidis. These fragments are derived from the full-length Tbp2 sequence by deletion, and the term "deletion" is recited in the claims. Thus, it is not true that the claimed product may be

derived by a "mental process" or by amino acid substitution, as asserted by the Examiner at page 7 of the Official Action.

Furthermore, these fragments are not made from any Tbp2 derivatives or variants. They are made exclusively from a naturally-occurring Tbp2 since the claims recite a N. meningitidis subunit and nothing more. Moreover, claims 54-78 are limited to fragments made by deleting in whole or part at least one domain, provided the first and second domains are not deleted simultaneously. In accordance with the present invention, these fragments are useful for vaccinal purposes since they are able to induce bactericidal antibodies against N. meningitidis.

In addition, the Examiner asserted that a deposit of the N. meningitidis strain IM2169 or IM2394 was required to enable the claims, and Applicants submit that such a deposit has been made, as described at page 19 of the present specification. Applicants will also prepare an appropriate affidavit with regard to this deposit and will submit such an affidavit at a later time.

Accordingly, Applicants submit that the Examiner's rejection under 35 U.S.C. § 112, first paragraph, is traversed for at least the foregoing reasons and should be withdrawn.

In the Official Action, the Examiner also rejected Claims 54-78 under 35 U.S.C. § 112, second paragraph, on the grounds that the Examiner deemed the term "maximal homology alignment" to be confusing, and on the grounds that the recitation of the term "stringent conditions" was unclear. With regard to the term "stringent conditions", Applicants have reviewed the claims but do

not see where this term is used, and thus the claims cannot be objectionable on this basis.

With regard to Applicants' use of "maximal homology alignment" and associated language in the claims, Applicants submit that these terms are clear on their face and are supported in the present specification at page 11, lines 5-13. In addition, Applicants submit that it is a relatively trivial task to align the two sequences so that the degree of identity or homology is maximum, as would be well understood by one of ordinary skill in this art. In fact, one skilled in this art would understand that there are simple computer programs that have been readily available on the market for a number of years which can achieve this result. Should the Examiner so desire, Applicants would be willing to set forth the foregoing information in the form of a Declaration.

Accordingly, Applicants submit that Claims 54-78 are proper in all respects under 35 U.S.C. § 112, and that the Examiner's rejections on the basis of this provision are respectfully traversed and should be withdrawn.

In the Official Action, the Examiner rejected Claims 54-77 under 35 U.S.C. § 102(b) as being anticipated by the Legrain et al. article, and rejected Claims 54-66 and 78 under 35 U.S.C. § 102(b) as being anticipated by the Quentin-Millet PCT published application WO 93/06861. Applicants submit that the present claims are not anticipated by these references and are patentable over them for at least the reasons as stated below.

With regard to the present application, Applicants' claimed invention relates to fragments of the Tbp2 subunit of the human transferrin receptor of N. meningitidis that have been found to be useful for vaccinal purposes. One class of useful fragments is constituted by Tbp2 fragments which comprise an amino acid sequence substantially corresponding to the first Tbp2 domain and further characterized in that the second or third Tbp2 domain is deleted in whole or part. A sub-class of useful fragments is constituted by fragments of the Tbp2 subunit of the IM2169 type which comprise an amino acid sequence substantially corresponding to the first Tbp2 domain and further characterized in that the Tbp2 immunodominant regions present in the second domain are deleted (see, for example, Claim 55). Fragments comprising the immunodominant region in which the N-terminal and C-terminal end (first and third domains, respectively) are deleted are also useful (see, e.g., Claim 76 and the specification at page 7, lines 23-24). The present invention as embodied by Applicants' claims 54-78 and described above is clearly not anticipated or made obvious by the references cited by the Examiner.

With regard to the Legrain et al. article, this article discloses the sequence of the DNA fragments encoding IM2169 (M982) and IM2394 (B16B6) Tbp2s as well as the full-length deduced amino acid sequences. In particular, the Examiner states that "it also discloses the tryptic peptide fragments of Tbp2 protein", citing page 74, paragraph bridging the left and right columns. In fact, the last paragraph in the first column mentions the full-length

Tbp1 (93 kDa) and Tbp2 subunits (68 kDa) purified from N. meningitidis strain B16B6 as well as the full-length Tbp1 (96 kDa) and Tbp2 (87 kDa) subunits of strain M982. This paragraph is thus irrelevant to the subject matter of the present claims insofar as it refers to full-length proteins.

Additionally, paragraphs on the top of the second column on page 74 reveal that the Tbps were submitted to tryptic digestion, and some of the tryptic peptides were purified and sequenced to validate the deduced Tbps amino acid sequences. However, these sequences are not provided at all in the Legrain article. Thus, although it may be theoretically possible to determine from the deduced Tbps amino acid sequences the sequences of all Tbps fragments that can be generated by trypsin digestion, a reader of this article is kept entirely in the dark regarding any fragments that may have been purified. There is no indication or suggestion whatsoever in the Legrain article that the purified tryptic fragments could correspond to the definition specified in Applicants' claims, and accordingly cannot anticipate or make obvious claims 54-78.

Even further, the Legrain article also mentions that Tbps are initially synthesized in the form of a precursor comprising a signal peptide (pre-peptide) that is cleaved upon secretion. However, Tbp2 signal peptides are different from the claimed Tbp2 fragments. Indeed these latter fragments are derived by deletion from full-length mature Tbp2s since the first, second and third domains, as recited by the present claims, exclusively cover mature

Tbp2s. A Tbp2 peptide signal, i.e., a peptide derived from a Tbp2 precursor by complete deletion of the first, second and third domain of the mature protein, cannot anticipate or make obvious claims 54-78 because these claims recite that the first and second domains are not totally deleted simultaneously.

Accordingly, Applicants submit that the present claims are clearly not anticipated or made obvious by the Legrain et al. article, and the Examiner's rejection on the basis of this reference is respectfully traversed and should be withdrawn.

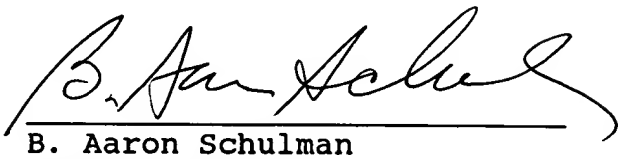
With regard to the Quentin-Millet PCT reference cited by the Examiner, this reference also does not anticipate or make obvious the present claims. This prior Quentin-Millet reference discloses a pharmaceutical composition comprising the Tbp2 subunits of N. meningitidis strains 2169 and 2394. However, this document only indicates in very general terms that immunogenic fragments of these Tbp2s may also be used instead of the full-length Tbp2 subunits, and does not disclose or suggest the Tbp2 fragments of the present invention. Accordingly, Applicants submit that the present claims are clearly not anticipated or made obvious by the prior Quentin-Millet PCT reference, and the Examiner's rejection on the basis of this reference is respectfully traversed and should be withdrawn.

Applicants thus submit that in light of the present amendment and arguments set forth above that the claimed invention is patentable over the references cited by the Examiner, and that the

application in its present form is in condition for immediate allowance. Such action is earnestly solicited.

Respectfully submitted,

November 14, 1997



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